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Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring

DOI:

[10.1016/j.dadm.2014.11.011](https://doi.org/10.1016/j.dadm.2014.11.011)

Published: 29/03/2015

Publisher's PDF, also known as Version of record

[Cyswllt i'r cyhoeddiad / Link to publication](#)

Dyfyniad o'r fersiwn a gyhoeddwyd / Citation for published version (APA):

Ciblis, A. S., Butler, M. L., Bokde, L. W., Mullins, P. G., O'Neill, D., & McNulty, J. P. (2015). Neuroimaging referral for dementia diagnosis: The specialist's perspective in Ireland.

Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring, 1(1), 41-47.

<https://doi.org/10.1016/j.dadm.2014.11.011>

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Neuroimaging referral for dementia diagnosis: The specialist's perspective in Ireland

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Abstract

Background: Neuroimaging is an increasingly important tool in the diagnostic workup of dementia. Neurologists, geriatricians, and old-age psychiatrists are involved in key tasks in the diagnostic process, frequently referring patients with suspected dementia for neuroimaging.

Methods: The research design was a postal survey of all geriatricians, old-age psychiatrists, and neurologists in the Republic of Ireland (N = 176) as identified by the Irish Medical Directory 2011–2012 and supplementary listings.

Results: Almost 65% of specialists did not have access to 2-[18F]fluoro-2-deoxy-D-glucose positron emission (FDG-PET) or FDG-PET/computed tomography (CT), and 80.3% did not have access to perfusion hexamethylpropyleneamine oxime single-photon emission computed tomography (SPECT) or dopaminergic iodine-123-radiolabeled 2β-carbomethoxy-3β-(4-iodophenyl)-N-(3-fluoropropyl) nortropane SPECT. Most specialists (88.7%) referred patients with mild cognitive impairment or suspected dementia for magnetic resonance imaging (MRI), 81.7% referred for CT, and 26.8% for FDG-PET or FDG-PET/CT. Only 44.6% of respondents were aware of dementia-specific protocols for referrals for neuroimaging.

Conclusion: Specialist access to imaging modalities other than CT and MRI is restricted. Improved access may affect patient treatment and care.

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Keywords:

Dementia; Neuroimaging; Geriatricians; Neurologists; Old-age psychiatrists; Access; MRI; CT; Nuclear medicine imaging

1. Introduction

Neuroimaging is increasingly regarded as an essential part of the investigation of a patient with suspected dementia [1]. Structural imaging has traditionally been used to exclude other cerebral pathologies in the assessment of suspected cases of dementia and to reveal findings consistent with Alzheimer's disease (AD) [2–4]. Some guidelines recommend its use in the evaluation of every patient with

suspected dementia [4]. Magnetic resonance imaging (MRI) is the preferred modality to assist with early diagnosis and detect subcortical vascular changes, however, computed tomography (CT) can also be used [2]. Treatable causes of dementia account for only a small proportion of all causes of dementia, however, and AD, vascular dementia (VaD), dementia with Lewy bodies (DLB), and frontotemporal dementia (FTD) are far more common causes [1,5].

With advances in technology, neuroimaging is now considered the most important ancillary investigation in the workup of dementia regarding differential diagnosis and management decisions [3,4,6,7]. Nuclear scans can help differentiate AD,

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VaD, and FTD if a diagnosis is unclear [7]. Guidelines by the National Institute for Health and Clinical Excellence/Social Care Institute for Excellence (NICE/SCIE) note that imaging may not always be needed for those presenting with moderate to severe dementia if the diagnosis is clear, and recommend the use of perfusion hexamethylpropyleneamine oxime (HMPAO) single-photon emission computed tomography (SPECT) or 2-[¹⁸F]fluoro-2-deoxy-D-glucose positron emission (FDG-PET) to distinguish between these subtypes if the diagnosis is in doubt [2]. In suspected cases of DLB, the use of dopaminergic iodine-123-radiolabeled 2 β -carbomethoxy-3 β -(4-iodophenyl)-N-(3-fluoropropyl) nortropane (FP-CIT) SPECT is recommended to confirm the diagnosis if it is in doubt [2].

FDG-PET is reimbursed in the United States for the distinction between AD and FTD [8,9]. In Ireland, PET scans are covered by the major private health insurance providers pending preapproval. FP-CIT (DAT-SPECT) is beneficial in the differentiation of DLB from AD and normal ageing [10]. Although SPECT and PET are not recommended for use as the only imaging measures, these modalities complement structural imaging where diagnostic uncertainty remains [4,11].

In AD, the most common form of dementia which accounts for approximately 60% to 70% of cases [12], atrophy in the medial temporal lobe, including the hippocampus, is an early and specific marker of the disease. Structural MRI imaging can determine volume loss in this region [1,13], and has been postulated as a marker for the progression of the disease [14,15]. The appearance of neuritic plaques is one of the neuropathological hallmarks of AD, the main constituent of which is the amyloid β protein. This protein is considered intrinsic to the pathogenetic process of AD and can be imaged in vivo using PET scans [16]. This allows for an early detection of the disease. Changes in brain metabolism can precede structural brain changes, and temporal, parietal, and posterior singular hypometabolism found in AD can be visualized using FDG-PET and help discriminate AD patients from controls [16]. FDG-PET scans show different patterns of hypometabolism in AD and FTD and can therefore assist in the differential diagnosis of the diseases [8].

At present, most people with dementia do not receive a formal diagnosis [17]. However, a specific diagnosis can influence treatment decisions, such as the use of acetylcholinesterase inhibitors in AD and DLB, the modification of vascular risk factors in VaD or carefulness in the use of neuroleptics in DLB or FTD [1]. Therefore, it would seem good patient management would make some imaging support for the diagnosis indispensable. The European Union (EU) joint action on Alzheimer's initiative, Alzheimer's cooperative valuation in Europe (ALCOVE) has identified four main professions as being responsible for most of the dementia diagnosis pathways: general practitioners, neurologists, geriatricians, and psychiatrists [6]. An exemplary pathway would have patients first recognized in primary care and subsequently referred to secondary care services such as a

memory clinic or directly to geriatricians, old-age psychiatrists, or neurologists, and would involve neuroimaging as an important part of this pathway.

In view of the underdiagnosis of dementia and the significance of neuroimaging in the diagnostic process, it is crucial that specialists have timely access to neuroimaging investigations and are confident in selecting the most appropriate modality. The present study investigated specialists' perspectives on access to neuroimaging investigations for suspected cases of dementia in Ireland and current referral patterns because adequate access and appropriate use of neuroimaging is required if diagnostic rates are to be improved.

2. Methods

2.1. Study design and participants

The research used a questionnaire-based study design. A postal survey questionnaire was addressed to all geriatricians, old-age psychiatrists, and neurologists in Ireland as identified through the Irish Medical Directory (IMD) 2011–2012. In addition, individual old-age psychiatrists, not contained in the IMD, were identified through a supplementary listing.

A total of 176 individual questionnaires were sent by post to the identified geriatricians ($n = 84$), old-age psychiatrists ($n = 46$), and neurologists ($n = 46$). Respondents were given 4 weeks to return the questionnaire. Returned survey sheets were completely anonymous and there was no follow-up.

2.2. Materials

The questionnaire consisted of five main sections and included both open and closed questions. Section A ascertained the demographic characteristics of the sample. Section B enquired about satisfaction with diagnostic capabilities within the health service and access to neuroimaging. Section C established specialists' current referral patterns in neuroimaging in dementia, their reasons for referral, and their use of protocols. Section D asked about the usefulness of reports on neuroimaging investigations.

2.3. Statistical analysis

Data analysis was carried out using IBM SPSS Statistics Version 20. Descriptive statistics are reported for most variables. Chi-square analysis including standardized residuals was performed to establish associations between categorical variables. Content analysis was used to examine open questions.

3. Results

3.1. Demographics

A total of 76 questionnaires were returned corresponding to a response rate of 43.2%. Over half of respondents (58.3%) were male. Most respondents (42.1%) were geriatricians, 28.9% were old-age psychiatrists and just over quarter

(26.3%) were neurologists. Most respondents (86.8%) were consultants.

The respondents' year of qualification ranged from 1972 to 2009 (8%, 1972–1981; 44%, 1982–1991; 41.3%, 1992–2001; 6.7%, 2002–2009). Neurologists were more likely to have qualified more recently (2002–2009; $\chi^2 = 21.81$, $P = .009$, standard residual [SR] = 3.4). The average number of years clinicians had spent in their current job was 7.8 years (standard deviation or SD = 5.95; range = 0.5–30 years).

Most participants (77.6%) worked in the public health service or under the Irish General Medical Scheme (GMS) which entitles patients with an income below a particular threshold to receive certain health services, including radiology examinations, free of charge. Another 11.8% worked in mixed practices, that is, in private practice and under the GMS. Just 10.5% worked in private practice only. Over half of respondents (57.4%) worked in county Dublin which is also a major urban area.

More than half of participants (54.1%) reported that most patients (75%–100%) were over 65 years of age, and 27% stated that between half and three quarters of their patients were of this age group. As expected neurologists were more likely to see younger patients, with half of them reporting that only 25% to 50% of their patients were aged more than 65 years ($\chi^2 = 49.82$, $P = .001$, SR = 3.7). Nearly all participants (97.4%) were involved in the diagnosis of mild cognitive impairment (MCI) or dementia.

3.2. Diagnostic capabilities within the health service area

Although about half of participants rated the proficiency in the diagnosis of MCI or dementia within their Health Service Executive region as excellent (4.1%) or good (46.6%), nearly 50% of respondents rated it as fair (39.7%) or poor (9.6%). There was no significant association between the geographic location that participants worked in and the rating of the capabilities ($\chi^2 = 7.03$; $P = .855$) or between specialization as geriatrician, old-age psychiatrist, or neurologist and the rating ($\chi^2 = 8.71$; $P = .191$).

Suggestions to improve the rate of diagnosis included, in order of frequency: better access to neuropsychology ($n = 23$), improved access to neuroimaging ($n = 18$), and better access to memory clinics ($n = 16$). A higher percentage of geriatricians (40.6%) cited better access to neuropsychology compared with old-age psychiatrists (23.8%) and neurologists (30%).

Most participants considered neuroimaging in dementia as important (46.1%) or very important (25%). There was no association between specialization and the reported importance of neuroimaging in dementia ($\chi^2 = 7.74$; $P = .560$).

3.3. Access to neuroimaging

All specialists reported that they had access to CT and MRI was available to most (see Fig. 1), however, nearly

two thirds of participants (64.5%) did not have access to FDG-PET or FDG-PET/CT and most respondents (80.3%) did not have access to HMPAO SPECT or FP-CIT SPECT. Although there was no significant association between specialization and reported availability of most neuroimaging modalities, there was a significant link between specialization and reported availability of FDG-PET or FDG-PET/CT whereby neurologists were more likely to have access to this modality than geriatricians or old-age psychiatrists ($\chi^2 = 7.94$; $P = .047$, SD = 1.7). There was no significant association between geographic location and the availability of the individual neuroimaging modalities.

3.4. Current referrals for neuroimaging

Nearly all respondents referred patients with MCI (90.8%) or suspected dementia (96.1%) for neuroimaging. MRI and CT were the most common forms of neuroimaging at 88.7% and 81.7% (no statistical difference, $t = -1.78$; $df = 70$; $P = .79$). Over a quarter (26.8%) referred these patients for FDG-PET or FDG-PET/CT. Only 4.2% referred for HMPAO SPECT and 11.3% for FP-CIT SPECT (Fig. 2).

Although there was no significant association between clinicians' specialization and the neuroimaging modalities they referred to overall, neurologists were more likely to report that they referred clients to FDG-PET or FDG-PET/CT ($\chi^2 = 9.62$; $P = .008$, SR = 2.2) and less likely to refer to CT ($\chi^2 = 14.77$; $P = .001$, SR = 2.8). There was no significant association between specialists' geographic location and the imaging modalities they referred to.

A total of 62.5% of respondents who referred patients for neuroimaging reported that there were modalities that they would like to have access to but that were unavailable to them. The modalities most frequently listed as unavailable were PET ($n = 17$), FDG-PET, or FDG-PET/CT ($n = 18$) and SPECT ($n = 18$). Again there was no significant link between specialists' geographic location and the unavailability of imaging modalities they would like to have access to ($\chi^2 = 20.61$; $P = .545$).

Most participants were either somewhat confident (54.8%) or very confident (32.9%) in selecting the most appropriate neuroimaging modality. There was no association between specialization and reported confidence

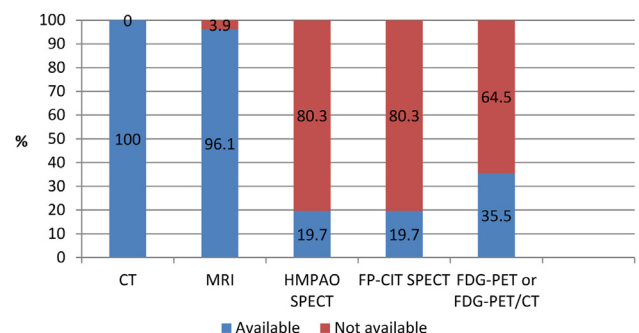


Fig. 1. Reported availability of neuroimaging modalities.

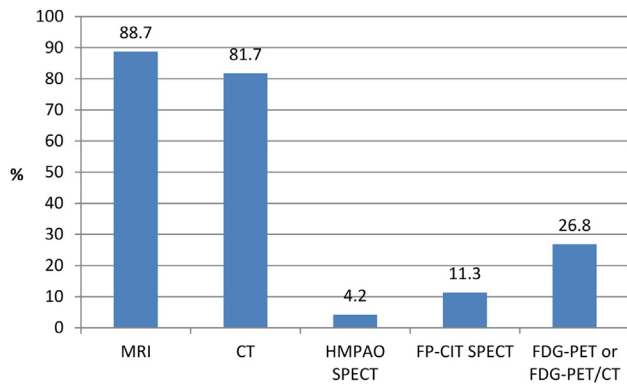


Fig. 2. Current referrals for the individual imaging modalities.

($\chi^2 = 6.75$; $P = .150$). The clear majority of respondents reported that they were very confident (13.2%) or somewhat confident (73.7%) in understanding neuroimaging in dementia. Most requests for neuroimaging were either never (45.9%) or rarely (41.9%) refused, and only 10.8% reported that they were sometimes refused. Reasons for a refusal included the inaccessibility of modalities, a lack of resources and funding, restrictions in health insurance coverage, and a questioning of the validity of the request by the radiologist. There was a significant association between neuroimaging refusal and referral for MRI. Respondents who referred to MRI were more likely to state that their referrals were quite frequently refused ($\chi^2 = 8.05$; $P = .045$, $SR = 2.6$). This association was not evident for the other imaging modalities. Factors not to request a scan included client characteristics such as frailty, advanced disease or clear diagnosis, and cost, a lack of availability of neuroimaging, and waiting times.

Less than half of respondents (44.6%) were aware of dementia-specific protocols for referrals for neuroimaging. There was no association between specialization and awareness of dementia-specific protocols ($\chi^2 = 2.41$; $P = .299$) or year of qualification and this awareness ($\chi^2 = 2.43$; $P = .486$). However, there was a significant association between referral of a patient under 65 years of age and awareness of dementia-specific protocols ($\chi^2 = 3.75$; $P = .044$), which was not found for other reasons for referral.

3.5. Reasons for referral

Specialists' reported reasons for referral for neuroimaging are displayed in Fig. 3. The question allowed for multiple responses. Most clinicians referred patients with suspected MCI or dementia for neuroimaging to rule out other causes (94.5%). A total of 69.9% referred to establish a differential diagnosis, and 63% referred to determine a dementia subtype. Just under half (46.6%) referred patients with suspected MCI or dementia for neuroimaging because the patient was under 65 years of age. Only 13.7% referred based on clinical guidelines such as the NICE/SCIE guidelines.

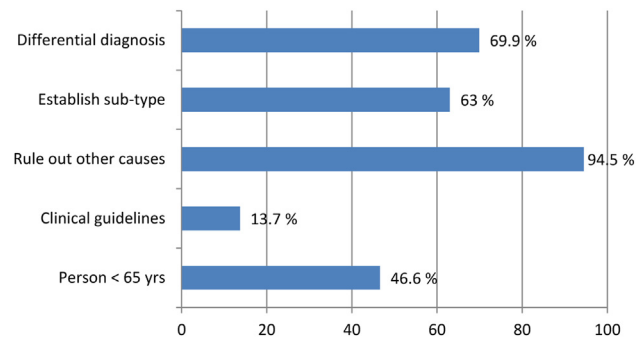


Fig. 3. Reported reasons for referral for neuroimaging.

There was an association between the rated importance of neuroimaging and referring patients to establish a differential diagnosis ($\chi^2 = 8.84$; $P = .031$) or a dementia subtype ($\chi^2 = 9.77$; $P = .021$) but not for any of the other reasons. No link was found between specialization and the reason for referral for neuroimaging.

3.6. Radiology report

Nearly all clinicians (97.4%) reported that they had access to reports on neuroimaging investigations about patients with suspected MCI or dementia. Most considered the information from the radiology report helpful (71.6%) or very helpful (17.6%) and rated their understanding of the report as good (71.6%) or excellent (12.2%). Those involved in explaining the report to patients and their family members found it easy (72.2%) or very easy (11.1%) to explain the information. There was no link between specialization and the reported usefulness of the radiology report ($\chi^2 = 6.59$; $P = .680$) or the perceived difficulty of explaining the report to patients ($\chi^2 = 7.53$; $P = .821$).

4. Discussion

Nearly half of respondents rated the proficiency in the diagnosis of MCI or dementia within their health service region as fair or poor. A lack of access to neuropsychological assessments, memory clinics, and neuroimaging investigations appeared to be key factors. Almost two thirds of participants stated that there were neuroimaging modalities that they would like to access but that were unavailable. These were mainly nuclear medicine imaging modalities, that is, PET and SPECT. Although most respondents referred patient with suspected dementia for neuroimaging to rule out other causes that are amenable to treatment, for which MRI or CT investigations are predominantly used [7,9], only approximately 1% to 10% of these investigations reveal reversible causes of dementia, and AD, VaD, DLB, and FTD are far more often the cause [4,5]. The results have shown that more than two-thirds of specialists referred suspected dementia cases to establish a differential diagnosis or a subtype diagnosis for which nuclear medicine investigations are frequently required. A subtype diagnosis is

important because it allows for a comprehensive care and management plan for patients and their families and helps those affected to know what to expect and which interventions might be beneficial [18]. Yet specialists' reported access to modalities other than CT or MRI was limited.

Nearly two-thirds of respondents reported that they did not have access to FDG-PET or FDG-PET/CT, and the overwhelming majority did not have access to HMPAO SPECT or FP-CIT SPECT in spite of the NICE/SCIE guidelines recommending the use of HMPAO SPECT, or FDG-PET, to help differentiate AD, VaD, and FTD [7]. The use of FP-CIT (DAT-SPECT) is recommended to confirm suspected cases of DLB [7] because it is beneficial in the differentiation of DLB from AD and normal ageing [4,9]. Although SPECT and PET are not recommended for use as the only imaging measure, these modalities complement structural imaging where diagnostic uncertainty remains and therefore constitute an important tool [4,11].

The higher percentage of referrals for FDG-PET compared with SPECT in the current sample may be related to recommendations such as the American College of Radiology appropriateness criteria for dementia which state that the differentiation between AD and VaD is better achieved using PET than SPECT investigations [19,20]. It might also be due to the higher reported availability of PET. According to a recent systematic review, PET appears to be superior to SPECT in identifying dementia subtypes and progression from MCI to AD although uncertainty remains in view of a lack of direct comparisons [21].

Almost three times as many specialists reported that they referred to FP-CIT SPECT compared with HMPAO SPECT though equal availability was reported. This could indicate the use of FP-CIT SPECT to aid in the diagnosis of DLB [10,19,22], because DLB is the second or third most common form of dementia [21] and HMPAO SPECT does not sufficiently differentiate between DLB and AD. Neurologists were found to be more likely to refer to FDG-PET or FDG-PET/CT and less likely to refer to CT than geriatricians or old-age psychiatrists. The slightly better reported accessibility to this modality for this group might be a factor and this could be because neurologists are generally presented with patients of different age groups and therefore more likely to require advanced imaging technology to diagnose various pathologies.

Although access to CT and MRI appeared to be adequate overall, a total of 4% of specialists did not have access to MRI in spite of its use being recommended over the use of CT in early diagnosis and detection of subcortical diagnosis in UK guidelines [7]. MRI increases specificity, and is preferable to CT for detecting vascular lesions in patients with dementia [4,19]. Moreover, CT has limited utility in the early detection of AD and in differentiating AD from other causes of dementia, whereas early changes in AD consistent with pathology (although not diagnostic in their own right) have been demonstrated using MRI [23]. Possible causes for the reduced availability of MRI in spite of its clinical ben-

efits include the higher cost associated with MRI in comparison to CT and its reduced insurance coverage, however, specialists still referred suspected cases of dementia more frequently to MRI than to CT in concordance with clinical guidelines. This is in line with results of the ALCOVE project which revealed that MRI was the most commonly used modality of medical imaging for dementia, except in late-stage dementia [6]. The specialists in this study reported that only 10% of their referrals to neuroimaging were refused. MRI referrals were found to be declined more frequently when compared with other modalities. This could be related to issues regarding accessibility and a lack of resources. Moreover, the use of CT might be considered adequate for certain investigations. Waiting lists which can run from weeks to months could also be a contributing factor [24].

The neuroimaging modalities that the specialists reported they would like to have access to but that were currently unavailable to them suggest that specialists are aware of advanced imaging modalities to aid in the diagnosis of dementia but are limited in their access. Specialists' expertise in the area is also reflected in their high reported confidence in selecting the appropriate neuroimaging modality and their high confidence in their understanding of neuroimaging in dementia.

The radiology report is often the main means of communication between the radiologist and the referring specialist. As such it must be easily understood, accurate, timely and appropriately detailed [25,26]. Its usefulness and current form have been debated, however. A recent survey of referring clinicians found that only 44.6% of specialists agreed that language and style of the radiology report were mostly clear, and only 41.4% considered the report important [27]. The use of structured reporting has been suggested but is debated [28]. The specialists in the current survey considered the radiology report sufficiently clear and useful. They reported no difficulties in explaining the information from the report to patients and their family members. This could indicate that the radiology report in its current form is sufficient for specialists to aid in the diagnosis of dementia.

In the absence of national clinical guidelines for the diagnosis of dementia it is not surprising that very few specialists reported referring patients with suspected dementia for neuroimaging based on guidelines. The creation of national guidelines has been called for, and the importance of such guidelines has been emphasized [29]. Likewise awareness of dementia-specific protocols for referrals for neuroimaging was low and would indicate a requirement for standardized protocols and further training in this area.

A strength of this study is the composition of the sample which was a good representation of the main specialists involved in the diagnosis of dementia [6]. The majority worked in the public health service and were thus representative of specialists in this area, however, less than half of the addressed specialists replied to the survey which could have introduced a bias.

5. Conclusion

Neuroimaging is an important tool in the diagnostic workup of dementia. With advances in imaging technology, it is no longer merely used to rule out other causes but also to assist in subtype diagnosis. This generally requires more advanced imaging modalities. Similar to other countries, the current research has revealed that access to modalities other than CT and MRI is limited [24,30]. This lack of access might impact on patient treatment and care. The provision of adequate access to neuroimaging is therefore imperative and an important step toward improving diagnostic rates.

Acknowledgments

The authors gratefully acknowledge the support of the participating specialists and Mr James Durkan for producing the database of specialists which facilitated the study. This study was part-funded by the European Regional Development Fund through the INTERREG 4A Ireland Wales Programme 2007–13. There is no conflict of interests.

RESEARCH IN CONTEXT

1. Systematic review: Literature searches were conducted using PubMed and Google Scholar to identify articles and guidelines on neuroimaging in dementia and its use by specialists.
2. Interpretation: Neuroimaging is considered an important tool in the diagnostic workup of dementia. Yet many specialists report inadequate access in particular to nuclear medicine scans which can be important in establishing a subtype diagnosis. A lack of access might therefore affect patient treatment and care.
3. Future directions: A comprehensive investigation of specialists' access to neuroimaging in dementia in other countries might further highlight the requirement for adequate access to neuroimaging investigations for suspected dementia patients to facilitate an accurate diagnosis and ensure appropriate treatment and care.

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